

REMARKS

Upon entry of this response, claims 1, 3-6, 15-19, 25, 26, 58, and 59 will be pending in this application. Claims 2, 7-14, 20-24, 27-57, 60, and 61 are cancelled. Claims 1, 15, and 16 have been amended to clarify the scope of the claims and delete reference to unelected subject matter. Claim 26 is amended to correct a typographical error. No new matter is added. Applicants respectfully request entry of the amended claims after final rejection, as the provided amendments relate to subject matter that has already been searched and would not require further consideration. Moreover, the amendments serve to place the application in condition for allowance or, alternatively, to focus any remaining issues for appeal.

Claim Rejections - 35 USC § 112

In the Office Action dated March 9, 2009, claims 1, 3-6, 8, 15-19, 25, 26, 55, 56, 58 and 59 were rejected under 35 U.S.C. 112, first paragraph, for failing to comply with the written description requirement. The Office alleges that one of skill in the art would not have understood the Applicants to have possession of the claimed subject matter at the time of filing because: 1) the modified M2-2 sequences covered by the claims do not comport with the scope of the disclosure and 2) the HMPV genome is highly variable.

The Applicants do not agree with the allegation that the present disclosure does not adequately describe the full scope of the previously claimed subject matter. Nonetheless, for the sole purpose of advancing prosecution and placing the claims in condition for allowance, the Applicants have cancelled claims 8, 55, and 56, and amended claims 1, 15, and 16 to limit the scope of the claims to mutations that ablate expression of the M2-2 protein. Applicants expressly reserve the right to pursue the full scope of these claims in one or more continuing applications. To the extent this rejection would be applied to the claims as amended, Applicants respectfully traverse.

In particular, Applicants note that as amended, the claims recite modifications that ablate (and not merely reduce) expression of the rHMPV M2-2 ORF. Applicants respectfully submit that the application as filed supports the full scope of the amended claims.

In this regard, Applicants respectfully disagree with the Office's allegation that the variability among various rHMPV strains renders the claimed subject matter inadequately

described. First, the relevant question – especially in light of the amendments to the claims – is not related to the degree of variability among the genomic nucleotide sequences of different HMPV strains, but instead whether the disclosed sequences for the M2-2 gene are sufficiently homologous to those of other HMPV strains to adequately describe the claimed subject matter. In this regard, an alignment of randomly selected HMPV M2-2 nucleotide sequences listed in GenBank indicates that the M2-2 sequences of strains 75 and 83 are highly reflective of the M2-2 genes that have been identified by others. Of the 8 randomly selected M2-2 sequences aligned to the M2-2 nucleotide sequence of strains 75 and 83, not one sequence was identified that did not have at least 95% identity to the M2-2 sequence disclosed for either strain 75 or strain 83. In particular, sequence comparisons showed that:¹

- GenBank accession number AY530089 is 95% identical to HMPV strain 75;
- GenBank accession number AY530090 is 97% identical to HMPV strain 83;
- GenBank accession number AY530091 is 97% identical to HMPV strain 83;
- GenBank accession number AY530092 is 95% identical to HMPV strain 83;
- GenBank accession number AY530093 is 97% identical to HMPV strain 83;
- GenBank accession number AY530094 is 95% identical to HMPV strain 75;
- GenBank accession number DQ843658 is 95% identical to HMPV strain 75;
- GenBank accession number FJ168779 is >99% identical to HMPV strain 83.

These findings indicate that the HMPV M2-2 protein is encoded by a highly conserved nucleotide sequence from strain to strain. Therefore, regardless of differences in the overall genomic sequences among HMPV strains (which may or may not exist to the level the Office alleges, as it cites no authority for this proposition), one of skill in the art would be able to readily identify the M2-2 protein of HMPV by performing a sequence analysis using the M2-2 sequences provided in the present application. After identifying the M2-2 protein, one of skill in the art could readily use the teachings of the present application

¹ Publicly available HMPV M2-2 sequences were identified using the National Center for Biotechnology Information nucleotide database (<http://www.ncbi.nlm.nih.gov/pubmed/>). Briefly, 16 nucleotide sequences for HMPV M2-2 were identified by searching the nucleotide database using the term “HMPV M2-2.” Eight of the sequences were randomly selected for sequence comparison with the M2-2 nucleotide sequences of strains 75 (SEQ ID NO.2, accession number AY297748) and 83 (SEQ ID NO.1, accession number AY297749) disclosed in the application; however, any sequences submitted by the Applicants were excluded from the analysis to assure that comparisons were not performed for the same virus sequence. Coincidentally, the majority of these sequences were submitted in 2004, and therefore, are representative of HMPV strains present at the time of filing.

to create an rHMPV having one or more mutations that ablate the expression of the M2-2 protein. Therefore, Applicants contend that the provided disclosure describes the full scope of the amended claims provided herein and respectfully request that the rejection under § 112, first paragraph, be withdrawn.

Claim Rejections - 35 USC § 103

Claims 55 and 56 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Birmingham *et al.*, 1999 (PNAS, Vol. 96, pp. 11259-11264, IDS) in view of van den Hoogen *et al.*, 2001 (Nature Medicine, Vol. 7, No. 6, p. 719-724, IDS) and van den Hoogen *et al.*, 2002 (Virology, Vol. 295, p. 119-132, IDS). The Applicants disagree with the Office's characterization of the cited art and the level of knowledge that one of ordinary skill in the art could derive from these references to arrive at the claimed subject matter with a reasonable expectation of success. However, for the sole purpose of advancing prosecution and placing the claims in condition for allowance, the Applicants have cancelled claims 55 and 56, without prejudice. Applicants expressly reserve the right to pursue the full scope of this canceled subject matter in one or more continuing applications.

Conclusion

Applicants respectfully submit that the pending claims, as amended, are patentable and request that a notice of allowance be issued.

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